7-22-86

CASWELL FILE

REFERENCE DOSES (RFDs) FOR ORAL EXPOSURE

Chemical: Naled (Dibrom)

CAS #: 380-76-5
Caswell #: 586

Carcinogenicity: No evidence of oncogenicity in two animal (mouse and rat) studies.

Systemic Toxicity: See below.

Preparation Date: 5/15/86

Endpoint	Experimental Doses	UF	MF	RfD
Bio-Research Lab. 1984	0.2 mg/kg/day ChE NOEL	10	10	0.002 mg/kg/day
2-Year Feeding/ Oncogenicity Rat Study	2.0 mg/kg/day ChE LEL			
brain ChE inhibition; Levels of 10 mg/kg/day showed slight RBC ChE inhibition, moderate plasma and brain ChE inhibition				

Endpoint and Experimental Doses:

Batham, P., Osborne, B.E., Bier, C., et al.
2-Year Feeding/Oncogenic Rat Study
Bio-Research Laboratories, LTD.
Study No. 9394; June 7, 1984

Sprague-Dawley CD rats were randomly assigned to 4 groups (55 animals/sex/group). The animals were fed (by gavage) diets containing 0, 0.2, 2, and 10 mg/kg/day for two years. Brain cholinseterase was inhibited approximately 24 and 60 percent in both male and female rats receiving dose levels of 2 and 10 mg/kg/day, respectively. Also there was a slight inhibition of red blood cell cholinesterase and moderate inhibiton of plasma cholinesterase at 10 mg/kg/day.

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Uncertainty Factors (UFs):

An uncertainty factor of 10 was used to account for the fact that a ChE NOEL was used in determining the RfD.

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Modifying Factors (MFs):

An additional MF of 10 to account for the lack of a complete data base which precludes the determination of the most sensitive toxicological endpoint.

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Additional Comments:

Data Considered for Establishing the RfD

1) 2-Year Feeding/Oncogenic - Rat ChE NOEL = 0.2 mg/kg/day, ChE LEL = 2.0 mg/kg/day (brain ChE inhibition); Systemic NOEL > 10 mg/kg/day; Oncogenic NOEL > 10 mg/kg/day; Levels of 10 mg/kg/day showed slight RBC ChE inhibiton, moderate plasma and brain ChE inhibition; core grade minimum

2) 2-Generation Reproduction - Rat Parental NOEL = 6 mg/kg/day, Parental LOEL = 18 mg/kg/day (decreased body weight in males); Progeny NOEL = 6 mg/kg/day, Progeny LOEL = 18 mg/kg/day (decreased survival, litter size and pup body weight); core grade minimum

3) Teratology - Rat Maternal NOEL = 10 mg/kg/day, Maternal LEL = 40 mg/kg/day (body weight loss, tremors, dyspnea and depressed activity); Teratogenic NOEL > 40 mg/kg/day (HDT); Fetotoxic NOEL > 40 mg/kg/day

4) Teratology - Rabbit Maternal NOEL > 8 mg/kg/day (HDT); Fetotoxic NOEL > 8 mg/kg/day (HDT); core grade supplementary

Data Gap(s)

1) Chronic Dog Feeding Study
2) Rabbit Teratology Study

Other Data Considered

1) 89-Week Feeding/Oncogenic - Mice Systemic NOEL = 15 mg/kg/day; Systemic LEL = 50-75 mg/kg/day (increased mortality, decreased body weight in males, decreased relative liver weight in females); core grade minimum

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Confidence in the RfD:

Study: Medium Data Base: Medium RfD: Medium

The critical study appears to be of fair quality and is given a medium rating. Since there are data gaps existing for naled, the RfD is given a medium confidence rating.

Documentation of RfD and Review:

Registration Standard, December 1982
Registration Files

Agency RfD Review:

First Review: 7/22/86
Second Review:
Verification Date: 7/22/86

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